# Spread of Discrete Structural Changes in Synthetic Polyanionic Gel: A Model of Propagation of a Nerve Impulse

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Thin fibers of cross-linked polyacrylate gel were prepared by inducing polymerization reaction inside long glass or Tygon tubings. By immersing these gel fibers in salt solutions containing both $Ca^{2+}$ and $Na^+$ at varying ratios, a discontinuous transition from the swollen state to the shrunken was demonstrated. A very sharp boundary was observed between the swollen and shrunken portions of the gel fiber. It was found possible to displace this sharp boundary continuously by application of a weak electric current. Based on the similarity in swelling behavior between nerve fibers and synthetic gel fibers, a non-myelinated nerve fiber carrying an impulse was treated as a cylindrical gel layer consisting of two distinct portions, a swollen (active) portion connected directly to the remaining shrunken (resting) portion. By applying the cable theory to this model of the nerve fiber, mathematical expressions describing the conduction velocity, the maximum rate of potential rise, etc. in terms of the electric parameters of the fiber were derived.

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## Introduction

During the past two decades, we have repeatedly demonstrated that the production of an action potential in the nerve fiber is invariably associated with rapid structural changes in the superficial layer of the fiber (Iwasa & Tasaki, 1981; Tasaki, 1999a, b). Specifically, we have found that nerve fibers swell during the rising phase and shrink during the falling phase of the propagated action potential. Since these rapid structural changes can be reversibly suppressed by substitution of $Na^+$-salt for the $Ca^{2+}$-salt in the surrounding solution, these changes are interpreted as being associated with the $Ca^{2+}$–$Na^+$ exchange process taking place in the superficial gel layer of the nerve fiber.

In the field of research of physical properties of synthetic polyanionic gels, it is known from the classical work of Katchalsky & Zwick (1955) that exchange of monovalent counterions in a polyanionic gel to divalent cations produces a drastic change in the degree of swelling of the gel. It is also known from the work of Tanaka (1978, 1981) that these changes in the degree of gel swelling can be wholly discontinuous. Such a discontinuous change in the gel structure is now considered to fully merit the term "phase transition". More recently, using small polyacrylate gel beads, we have shown that a discontinuous volume transition can be induced in the gel by an extremely small change in the $Ca^{2+}$–$Na^+$ concentration ratio in the external solution (Tasaki & Byrne, 1992).

In these circumstances, it is expected that a close investigation into the mechanism of

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swelling in chemically well-defined polyanionic gels, preferably under physiologically significant experimental conditions, will lead to a better understanding of the analogous cation-exchange process taking place in intact, excitable, nerve fibers. On these grounds, the present study was initiated with a view toward elucidating the mechanism by which structural changes are induced in nerve fibers by studying the process of swelling and shrinking in synthetic polyanionic gels.

It is known that the superficial gel layer of a nerve fiber contains filamentous macromolecular elements (microtubules, actin filaments, etc.) which undoubtedly carry fixed negative charges under physiological conditions (see Metuzals, 1969; Tsukita et al., 1986). For the reason that nerve fibers have the shape of an elongated cylinder, thin fibers of polyanionic gel—cross-linked polyacrylate gel fibers—were employed in the study. Using a dissecting microscope with provision for dark-field illumination, the patterns of initiation and propagation of the structural changes in the gel were examined.

The results obtained were interpreted as giving an additional support to the phase-transition paradigm formulated to explain the mechanism of propagation of an impulse in the nerve fiber (Tasaki, 1982, 1999a, b; Pollack, 2001). Extending the previous work by Matsumoto & Tasaki (1977), some mathematical consequences of this paradigm are presented in Appendix A.

It should be remarked in this connection that, in this article, the behavior of the nerve fiber is described solely in terms of the coarse-grained variables, without reference to the microscopic details of the system (see also Tasaki, 1999a). In other words, the approach adopted here does not yield any information about the processes taking place in individual intrinsic membrane protein molecules or transmembrane cation pathways (ion channels).

## Material and Method

The preparation of polyanionic gel fibers began with partial neutralization of 30 g of acrylic acid (Aldrich Chem. Co.) with 12 g of NaOH dissolved in 100 ml of distilled water. Next, 100 mg of $N, N'$-methylene-bis-acrylamide (Sigma Chem. Co.) was added to the Na-acrylate solution and, by stirring the solution with bubbling nitrogen gas, this cross-linker was completely dissolved in the solution. The preparation of pre-gel solution was completed by addition of 90 mg of ammonium persulfate (Aldrich Chem. Co.), the initiator, to the solution. Then, by use of a fine hypodermic needle and a syringe, the pre-gel solution was drawn into glass capillaries or Tygon microbore tubings (S-54-HL) of which the inside diameter ranged between 0.5 and 0.25 mm. Gelation—the formation of cross-linked Na-polyacrylate—was achieved by keeping the temperature of the tubings filled with the pre-gel solution at about 78°C for 1 h.

In order to remove unreacted chemical elements from the newly synthesized gel, short pieces of gel-filled tubings (10–20 mm in length) were placed in a large Petri dish filled with distilled water. As is well known, sorption of water by the gel brings about an over 200-fold expansion of the gel volume. When a gel-filled tubing is immersed in distilled water, massive gel expansion takes place in the vicinity of the two openings of the tubing, leading to formation of a long strand of swollen gel at each end of the tubing. Therefore, simply by immersing the gel-filled tubings in distilled water, the transfer of the major portion of the gel from the tubings to distilled water could be accomplished in 1 day or 2.

The changes in the structure of the gel associated with $Na^+$–$Ca^{2+}$ exchange were examined in most of the present studies by using a Bausch and Lomb dissecting microscope provided with 1.3, 3 and $7.5 \times$ objective lenses. A beam of light from an incandescent lamp was focused on the gel fiber in a vessel on the microscope stage from below. On several occasions, a Zeiss otoscope was also used in the study. Photomicrographs were taken by use of a Polaroid MicroCam SLR camera.

## Results

### DISCONTINUOUS VOLUME TRANSITION IN THIN GEL FIBERS

As stated above, we have already seen that, in small spherical beads of polyacrylate gel, a discontinuous volume transition can be
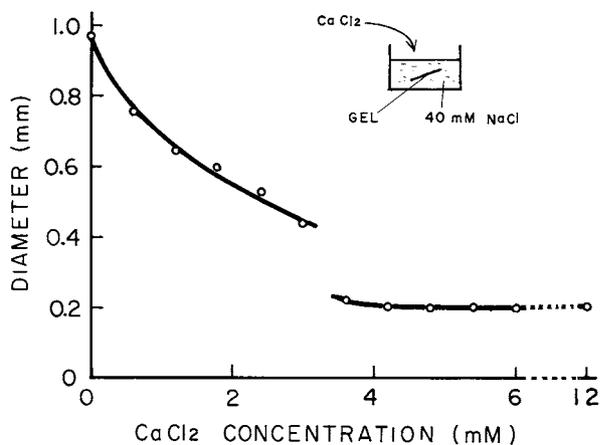
FIG. 1. Discontinuous diameter change in cross-linked polyacrylate gel fiber induced by $CaCl_2$ added to the external 40 mM NaCl solution, plotted against the external $CaCl_2$ concentration. The gel was synthesized inside a Tyson microprobe tubing of 0.25 mm inside diameter (22°C).

produced by a $Ca^{2+}$–$Na^+$ exchange. In the present study, we show that this type of structural change can also be induced in thin fibers of polyanionic gel (see Fig. 1).

A long fiber of $Na^+$-polyacrylate gel, approximately 1 mm in diameter in its swollen state, was cut down to 12 short pieces of about the same length. Each piece of the gel fiber was placed in a glass vessel containing a 40 mM NaCl solution whose pH was kept at about 7.4 (HEPES buffer). Then, after adding small aliquot portions of a concentrated $CaCl_2$ solution to the vessels, the diameter of each fiber was repeatedly measured until equilibrium was reached between the gel and the surrounding salt solution.

It is seen in the figure that, in the range of concentration below a certain critical level (about 3 mM in the present case), the diameter of the fiber decreased continuously with the $Ca^{2+}$-concentration in the vessel. At the critical $CaCl_2$ concentration in the vessel, the diameter was found to decrease by a factor of about 1/2. In the range of the $Ca^{2+}$- concentration exceeding the critical level, no progressive decrease was observed in the diameter with rising $Ca^{2+}$-concentration outside the gel. The diameter of the gel fiber in this shrunken state was only about 3/4 of the inside diameter (0.25 mm) of the tubing in which the gel was synthesized.

The shrinking process induced by $Ca^{2+}$ was reversible. When the surrounding $Ca^{2+}$-containing salt solution was replaced with a $Ca^{2+}$-free, NaCl solution, swelling of the gel fiber began after some delay, and the fiber eventually returned to the size determined by the equilibrium between the fiber and the solution. Qualitatively, there seemed to be little difference in the swelling behavior between beads and fibers of cross-linked polyacrylate gel.

### SPREAD OF STRUCTURAL CHANGES IN SUPERFICIAL LAYER OF SHRUNKEN GEL INDUCED BY REMOVAL OF CA$^{2+}$

When a fiber of cross-linked polyacryate gel in its shrunken state was transferred to a 40 mM NaCl solution (free of $Ca^{2+}$), the superficial layer of the fiber began to swell after a delay of 5–20 min. Assuming that the origin of this delay is similar to that of solid-state physicists' induction period (see Russell, 1980), it is suggested that this represents the time required for establishing a steady nucleation condition necessary for the swelling process in the gel.

The first visible sign of a change in the gel structure induced by the removal of $Ca^{2+}$ in the medium was the appearance of a fine, more-or-less regular polygonal pattern on the surface of the gel (see Fig. 2). Frequently, such a pattern appeared first in the immediate vicinity of the cut end of a shrunken gel fiber and then gradually propagated along the gel surface. At the outset, the size of the individual polygon in the pattern was about $10^{-6} cm^2$ or less. The pattern was progressively coarsened by the disappearance of the walls between neighboring polygons. Usually, between 10 and 30 min after the onset of the visible structural change, the entire surface of the fiber was covered with a thin layer of swollen gel. Finally, the process of swelling spread inwards until the entire fiber assumed its swollen state.

### SPREAD OF STRUCTURAL CHANGES ALONG THIN FIBERS OF POLYANIONIC GEL

In the first series of experiments along this line, the spread of shrinkage along the interior of a thin fiber of cross-linked polyacrylate gel was examined using the setup schematically illustrated in Fig. 3, top. A long gel fiber, which
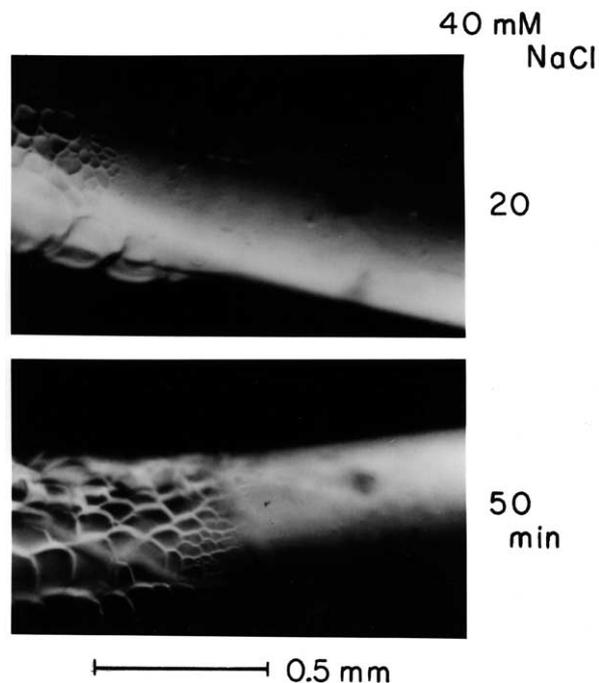
40 mM
NaCl

20



50
min

|——————————| 0.5 mm

FIG. 2. Structural change at the surface of a cross-linked polyacrylate gel fiber in its shrunken state, induced by removal of $Ca^{2+}$ in the external medium. The gel fiber employed was kept overnight in a solution containing 4 mM $CaCl_2$ and 40 mM NaCl. The photomicrographs were taken following transfer of the fiber to a 40 mM NaCl solution at the time indicated (22°C).

was synthesized inside a 0.25 mm (i.d.) Tygon microbore tubing, was kept in its swollen state by immersion in a 40 mM NaCl solution (pH 7.4). Then, the fiber was transferred to a platform consisting of two glass plates, each roughly 5 cm square, separated by a narrow (1–2 mm wide) gap. One of the glass plates was used to hold a pool of the NaCl solution and the other plate was for accommodating a dilute (27 mM) $CaCl_2$ solution. The gel fiber was placed on the platform in such a manner that about one-half of the fiber was immersed in the $CaCl_2$ solution and the remaining half was kept in the NaCl (i.e. $Ca^{2+}$-free) solution.

In this environment, the portion of the fiber placed in the $CaCl_2$ solution began to shrink and soon, in the vicinity of the gap between the two plates, a sharp boundary was formed, separating the shrunken portion of the fiber from the swollen portion. When a weak electric current was applied to the portion of the gel fiber crossing the air-gap under these conditions, it

−                +

40 mM NaCl          27 mM CaCl$_2$
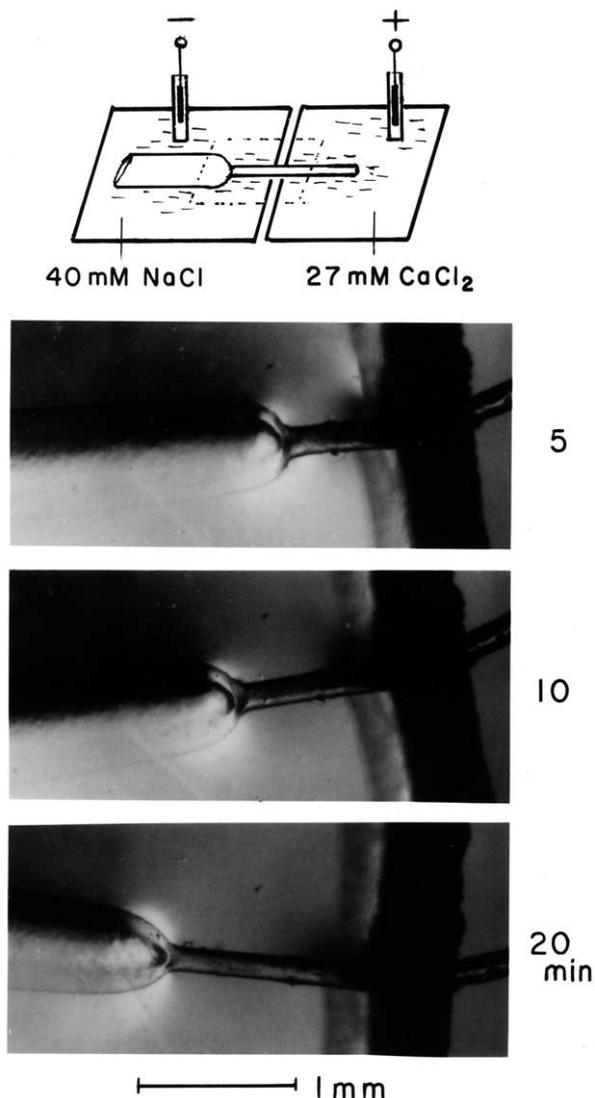


5

10

20
min

|——————————| I mm

FIG. 3. Spread of shrinkage along the swollen portion of a thin fiber of cross-linked polyacrylate gel. Top: Schematic diagram of the experimental setup employed. The numerals indicated in the figure represent the time after the onset of the electric current. Note the sharpness of the boundary between the shrunken and swollen portions of the gel fiber (see text).

was found that the sharp boundary between the swollen and shrunken portions started to migrate in the direction of the current flow.

The photomicrographs furnished in Fig. 3 were taken by delivering an electric current of about 70 μA (DC) directed from the $CaCl_2$ side to the NaCl side of the air-gap. (Note that the current intensity is determined by the voltage applied between the two pools and the resistance of the shrunken portion of the fiber bridging the
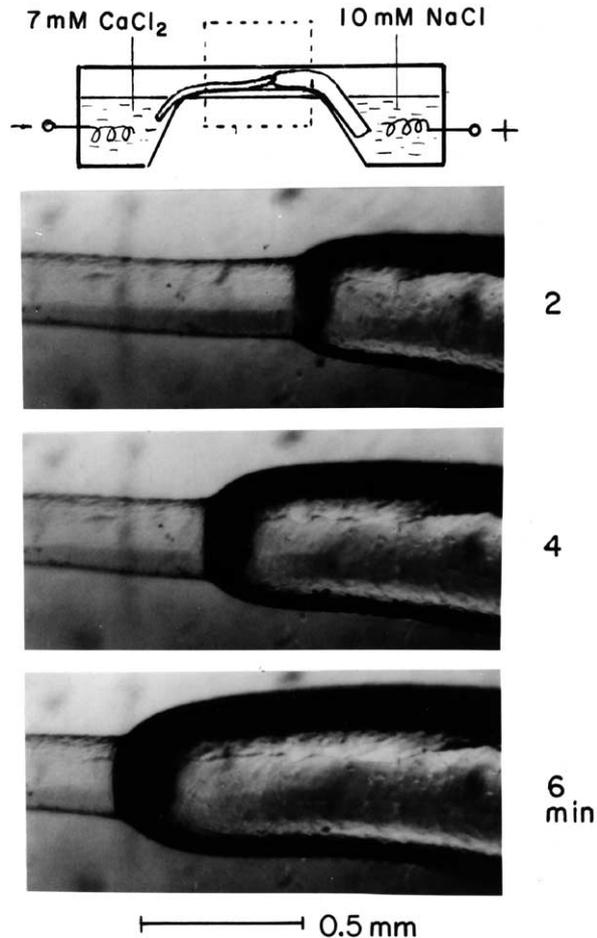
FIG. 4. Spread of swelling into the shrunken portion of a thin fiber of cross-linked polyacrylate gel. The experimental arrangement employed is schematically illustrated at the top. The photomicrographs were taken at the time indicated after the onset of electric current. Note that the boundary between the swollen and shrunken portions of the gel fiber remained sharp (see text).

gel fiber was examined. Here, the setup employed (see Fig. 4, top) consisted of a 10 mm wide platform separating two pools of salt solutions. A long gel fiber in its shrunken state was stretched across the platform, introducing a portion of the fiber near one end into a $Ca^{2+}$-rich solution and the portion near the other end into a $Ca^{2+}$-free solution. After raising the surfaces of the two solutions close to the flat top level of the platform, the upper surface of the gel fiber was covered with a thin layer of mineral oil. Shortly afterwards, there was a rapid swelling of the portion of the fiber immersed in the $Ca^{2+}$-free, NaCl solution. Under these conditions, using a pair of Ag–AgCl electrodes immersed in the salt solutions, the effect of an electric current applied to the fiber was examined under a dissecting microscope.

When the current (of about 1 mA) was directed from the $Ca^{2+}$-free side toward the $Ca^{2+}$-rich side, there was a gradual expansion of the swollen portion into the shrunken portion of the fiber. Under these experimental conditions, there was a thin layer of salt solution on the top of the platform and an appreciable portion of the applied current was expected to flow outside the fiber. (Note that the resistivity of the swollen gel was roughly 200 $\Omega$ cm.) Nevertheless, the process of exchange of $Na^+$ for $Ca^{2+}$ induced in the gel by the applied current was found to bring about a gradual displacement of the boundary toward the cathodal side of the fiber. Again, the boundary between the swollen and shrunken portions remained very sharp.

## Discussion

The structure of an excitable (living) nerve fiber is quite different from that of synthetic polyacrylate gel fiber used in the present studies. Nevertheless, the experimental arrangements schematically illustrated at the top of Figs 3 and 4 were designed to reproduce the process of critical importance involved in nerve excitation and conduction. The process in question is the monovalent–divalent cation exchange associated with the flow of electricity.

There is no question that internally perfused squid giant axons have best served for the illustration of the process of nerve excitation

air-gap. Note also that the applied current tends to steadily increase the quantity of $Ca^{2+}$ carried across the gap.) It is seen in the figure that the boundary between the swollen and shrunken portions of the fiber was moving steadily along the portion of the fiber in the NaCl solution. As expected, the rate at which the boundary was displaced along the fiber varied with the intensity of the applied current. It is of deep interest to us that, during the entire period of these observations, the boundary between the swollen and shrunken portions remained quite sharp.

In the second series of experiments along this line, the process that leads to spreading of the swelling process into the shrunken portion of a

and conduction. In these axons, the major portion of the cytoplasmic gel inside was surgically and enzymatically removed, leaving a superficial gel layer of a few μm in thickness untouched. The ability to produce propagated nerve impulses is preserved in these axons for many hours, when favorable salt solutions are chosen inside and outside the axon (Tasaki, 1982). In these axons, solutions of the salts of $Ca^{2+}$ and its substitutes ($Sr^{2+}$ or $Ba^{2+}$) are favorable outside the axon. Without being accompanied by $Ca^{2+}$ or its substitute, the salt solution containing only $Na^+$ in the external medium is totally inadequate to keep the axon excitable.

In axons immersed in a $Ca^{2+}$-containing external solution and internally perfused with a solution containing only monovalent cations, an electric current passing through the superficial gel layer brings about an immediate change in the divalent–monovalent cation ratio in the gel layer. It is to be noted that, in an axon carrying an impulse, there is an outwardly directed current through the superficial gel layer during the early period of the action potential (see Appendix A). According to the old principle in neurophysiology originated with Ludimar Hermann (see Tasaki, 1982, pp. 32 and 50), it is this outwardly directed current through the resting membrane that serves to trigger the excitation process in the axon.

In the field of physicochemical research of polyanionic macromolecules, it is known that the strong electrostatic interaction between divalent cations and polyanion leads to specific association between macromolecules and divalent cations (see, e.g. Ikegami & Imai, 1962, p. 147; Katchalsky, 1971, p. 147; Oosawa, 1971, p. 56). These researchers have suggested the formation of uncharged complex when polyanionic macromolecules are immersed in $Ca^{2+}$-rich media. Thus, it appears reasonable to assume that the superficial gel layer of the nerve fiber immersed in physiological salt solutions (containing $Ca^{2+}$) is stabilized by the formation of such uncharged complexes, and further, that a transition from the resting to the active state of the layer involves breakage of such complexes.

The microphotographs presented in Figs 3 and 4 suggest that the structural changes occurring in nerve fibers can also have a discontinuous feature. The photomicrographs in Fig. 2 appear to give a new insight into the process of excitation of a nerve fiber evoked by threshold stimuli.

Some of mathematical consequences of the discrete structural changes in the non-myelinated nerve fiber are discussed in Appendix A.

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## Appendix A

## A Study of Nerve Conduction by Use of Cable Equation

In this Appendix, we demonstrate that various properties of the non-myelinated nerve fiber, such as, the conduction velocity, the maximum rate of potential rise, etc., can be deduced solely from the consideration of the discontinuity between the active (swollen) and resting (shrunken) zones. Here, there is no requirement for the information about the time-dependent changes in the membrane resistance and e.m.f. Furthermore, the nature of the ionic process that serves to maintain the membrane resistance and e.m.f. is immaterial to the present analysis.

The electrical properties of a nerve fiber carrying an impulse can be represented by an electric network illustrated in Fig. A1. This network consists of two distinct zones, active and resting. In the resting zone, the electric resistance of the membrane (surface layer) of the fiber, $r_m$, is relatively high. The membrane resistance in the active zone, $r_m^*$, is low. The e.m.f. of the membrane in the resting zone, $E_r$, makes the potential of the nerve interior negative; the polarity of the e.m.f. in the active zone, $E_a$, is opposite. The longitudinal (cytoplasm) resistance, $r_i$, and the membrane capacity, $c_m$, are nearly the same in these two zones.

The behavior of this type of electric network has been studied previously by Matsumoto & Tasaki (1977). In the previous study, the existence of a "transitional zone" with a finite length between the active and resting zones was assumed. The experimental findings described under Results of this article suggest that this assumption is unnecessary. When the two zones are connected directly (i.e. without inserting a transitional zone), the membrane potential at the boundary between the two zones, which was not definable previously, becomes a well-defined quantity. Nevertheless, as will be shown below, the findings described previously remain valid.

It is well known (see, e.g. Offner *et al.*, 1940) that the electric potential at position $x$ and time $t$, $V(x, t)$, in the resting zone of the fiber can be described by the following equation:

$$c_m \frac{\partial V}{\partial t} + \frac{1}{r_m}(V - E_r) = \frac{1}{r_i}\frac{\partial^2 V}{\partial x^2} \quad \text{(A.1)}$$

(see Fig. A1). When we are dealing with the case where a nerve impulse is traveling at a constant velocity $v$ in the positive direction of $x$. Equation (A.1) can be simplified by introducing a new variable $X$ defined by $X \equiv (x - vt)$:

$$\frac{1}{r_i}\frac{d^2 V}{dX^2} + c_m v \frac{dV}{dX} - \frac{1}{r_m}(V - E_r) = 0. \quad \text{(A.2)}$$
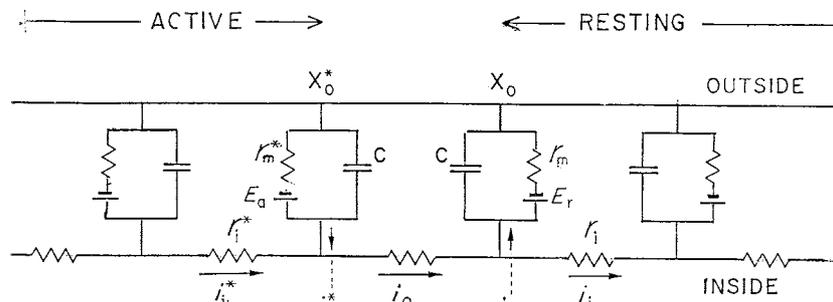


FIG. A1. Electric network representing the condition of a non-myelinated nerve fiber in the vicinity of the boundary between the active (excited) and resting zones. The fiber is immersed in a large volume of salt solution with low resistivity. The symbols denote the following parameters; $r_m$, membrane resistance for unit length of the fiber; $c_m$, membrane capacity per unit length: $E_a$ and $E_r$, membrane e.m.f. in the active and resting zone, respectively; $i_m$, membrane current per unit length; $i_i$, longitudinal current; $i_o$, longitudinal current at the boundary. The asterisk indicates the parameters in the active zones. $X_0^*$ and $X_0$ represent the ends of the active and resting zones, respectively.

The solution of this equation is

$$V = E_r + (V_0 - E_r)e^{-\xi(X-X_0)}, \qquad \text{(A.3)}$$

where $V_0$ represents the value of $V$ at the beginning of the resting zone, $X_0$, and $\xi$ is given by

$$\xi = \frac{c_m v + \sqrt{(c_m v)^2 + 4/(r_i r_m)}}{2/r_i}. \qquad \text{(A.4)}$$

Analogously, the cable equation for the active zone of the axon and its solution are

$$c_m \frac{\partial V}{\partial t} + \frac{1}{r_m^*}(V - E_a) = \frac{1}{r_i}\frac{\partial^2 V}{\partial x^2} \qquad \text{(A.5)}$$

and

$$V = E_a + (V_0^* - E_a)e^{+\eta(X-X_o^*)}, \qquad \text{(A.6)}$$

where $V_0^*$ is the potential at the advancing end of the active zone, $X_0^*$, and $\eta$ is given by the following equation:

$$\eta = \frac{-(c_m v) + \sqrt{(c_m v)^2 + 4/(r_i r_m^*)}}{2/r_i}. \qquad \text{(A.7)}$$

Note that the active zone is assumed to extend from the boundary to $-\infty$. This assumption is justifiable when the active zone is much longer than $1/\eta$.

At the boundary, both $V(X)$ and its derivative are continuous. Furthermore, we have the following relation between the membrane current at the beginning of the resting zone, $i_m$, and the longitudinal currents, $i_o$ and $i_i$.

$$i_m = (i_o - i_i).$$

The corresponding relation at the advancing end of the active zone,

$$i_m^* = (i_i^* - i_o).$$

[Note that $i_m$ is outwardly directed (positive) and $i_m^*$ is inwardly directed (negative).]

Under these boundary conditions, it was found possible, after some algebraic operations involving repeated squaring, to derive the following compact equation relating the conduction velocity, $v$, to the electric parameters of the nerve fiber:

$$v = \frac{1}{c_m\sqrt{2r_i r_m^*}}\sqrt{\frac{(1-\kappa)^2}{1+\kappa}}, \qquad \text{(A.8)}$$

where $\kappa$ denote the ratio of the membrane resistance in the active state to that in the resting state, $r_m^*/r_m$ (see Matsumoto & Tasaki, 1977). Since this ratio is usually far smaller than unity in normal nerve fibers, eqn (A.8) can be simplified further:

$$c_m v = (2r_i r_m^*)^{-1/2}. \qquad \text{(A.9)}$$

In the present case, $V_o = V_o^*$ at the limit $\Delta X \to 0$. Introducing eqns (A.3) and (A.6) into the condition of continuity of $dV/dX$ at the boundary, and then simplifying by use of eqn (A.9), we find that

$$\frac{E_a - V_o}{V_o - E_r} = \frac{\xi}{\eta} = \frac{1 + \sqrt{1+8\kappa}}{2} \approx 1. \qquad \text{(A.10)}$$

Equation (A.10) indicates that the inflection point in the rising phase of the potential, $V$, associated with a propagated impulse is located near the midpoint of the rising phase.

The rate of potential rise at the moment $V_o$ is reached, which is maximal, can be obtained by differentiating $V$ in eqn (A.3) with respect to $t$:

$$-v\frac{dV}{dX}\bigg|_{X_0} = (V_0 - E_r)v\xi = \frac{(E_a - E_r)}{4CR^*}, \qquad \text{(A.11)}$$

where $C$ and $R^*$ denote the capacity and resistance of the membrane in the active state expressed in $\text{F cm}^{-2}$ and $\Omega\,\text{cm}^2$, respectively, the product $CR^*$ being the time constant of the membrane in its active state.

Next, the factors that determine the conduction velocity, $v$, are examined. Expressed in terms of C and $R^*$, eqn (A.9) becomes

$$v = \sqrt{\frac{d}{8\rho C^2 R^*}}, \qquad \text{(A.12)}$$

where $\rho$ is the specific resistance of the interior of the nerve fiber and $d$ is the fiber diameter. The proportionality of $v$ to the square root of $d$ is known from the theoretical work of Offner et al. (1940), Rushton (1951) and others. The dependence of $v$ on the square root of $\rho$ is in

accord with the theory of Offner *et al.* Using squid giant axons internally perfused with $K^+$-salt solutions, Matsumoto & Tasaki (1977) have demonstrated that eqn (A.12) adequately describes the dependence of the conduction velocity $v$ on the membrane resistance at the peak of excitation, $R^*$, and the resistivity of the internal solution, $\rho$. It is to be noted that no adjustable parameter was used in this case. Note also that no precise knowledge of the membrane e.m.f.s was required here.

As is well known, Hodgkin & Huxley (1952) were able to calculate the entire time course of a propagated action potential on the basis of their sodium theory. In their calculation, a precise knowledge of voltage and time dependence of the conductances, was required. The peak value of the sodium conductance in their theory corresponds to $1/r_m^*$ in the present treatment. It may be noted here that, in squid giant axons internally perfused with $K^+$-salt solution, $1/r_m^*$ varies, to a considerable extent, with the internal $K^+$-concentration (Matsumoto & Tasaki, 1977, Table 1). This is what is expected from the cation-exchange property of the swollen superficial layer of the axon.

Finally, we consider the cases in which the membrane resistance in the active state, $r_m^*$, does not fall far below the resting membrane resistance, $r_m$. Such depressed excitability is encountered in lightly anesthetized nerve fibers. A rise in $r_m^*$ brings about an increase in the "space parameters", $1/\eta$. The fall in the conduction velocity $v$ in such fibers is adequately described by eqn (A.8). From eqn (A.11), a marked fall in the rate of the potential rise is expected. As in the case of anesthetization of a myelinated nerve fiber (Tasaki, 1982, p. 83), nerve conduction is expected to be suspended when the length of the region traversed by outward current, $1/\xi$, becomes comparable to the length of the active zone.

In conclusion, the results of the present analysis of the cable equation are summarized as follows: (1) The rapid structural change in the superficial gel layer of the nerve fiber plays a crucial role in the process of nerve conduction. (2) By treating a non-myelinated axon carrying an impulse as a thin cylindrical layer of polyanionic gel, the process of nerve conduction was analyzed on a quantitative basis. (3) The dependence of the conduction velocity [see eqn (A.12)], the maximum rate of potential rise [see eqn (A.11)], etc. on the electric parameters of the superficial gel layer was clarified.